Improving Cross-linking of Degradable Thiol-acrylate Hydrogels via Peptide Design

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Hydrogels fabricated from poly (ethylene glycol) (PEG) based macromers are ideal for drug delivery and tissue engineering applications. Recently, a new visible light-mediated photopolymerization scheme was developed to fabricate cytocompatible and degradable poly (ethylene glycol)-diacrylate (PEGDA) hydrogels. Co-polymerization of mono-cysteine peptides (e.g. CRGDS) with PEGDA offers the gels with cell adhesion property. However, this approach causes significant reduction in network crosslinking density, in part due to chain transfer of thiols to acrylates. The goal of the project is to improve the network cross-linking efficiency of this peptide-immobilized PEGDA hydrogel for cell culture. We hypothesized that the incorporation of bi-functional bis-cysteine peptides or silk fibroin will produce hydrogels with enhanced stiffness. The shear moduli of the gels were characterized via oscillatory rheometry in strain-sweep (0.1-5%) mode. Hydrolytic degradation of the gels as a function of time was also evaluated by rheometry. Cytocompatibility of the hydrogel system will be assessed by in situ encapsulation of 3T3 fibroblasts. Cell metabolic activity was determined by Alamar-Blue assay. We found that the bis-cysteine peptide enhanced gel crosslinking, as compared with mono-cysteine peptide. Incorporation of silk fibroin protein also exhibited enhancement in gel stiffness. However, the optimum concentration of incorporated silk fibroin presented an increased shear modulus compared to gels containing only the mono-cysteine peptide. Ongoing work is focused on fine-tuning gel formulations and degradation, as well as on evaluating the cytocompatibility of these visible-light cured thiol-acrylate hydrogels.

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